

Experience in Aligning Anatomical Ontologies



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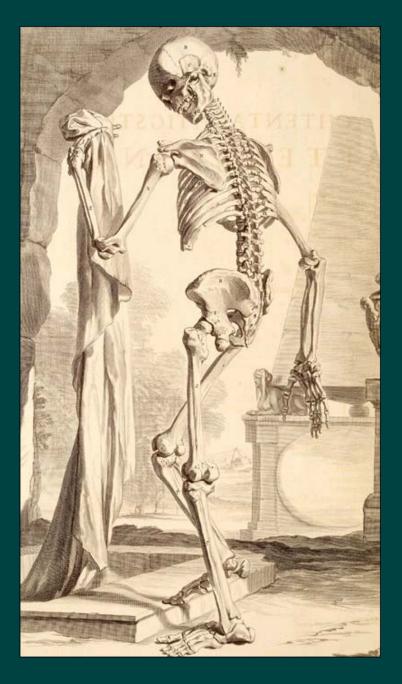
Acknowledgments



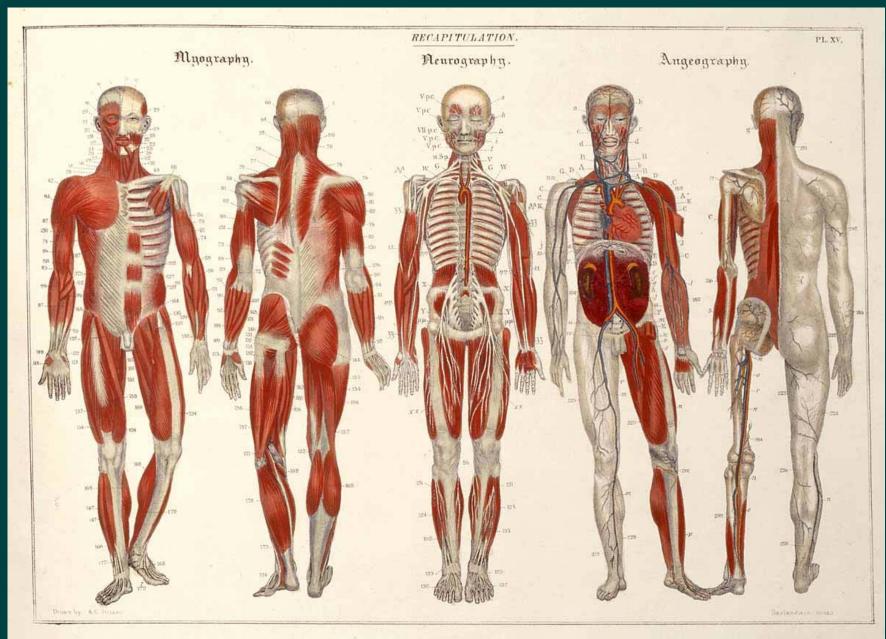


- ◆Songmao Zhang
 - National Library of Medicine, USA
 - Academy of
 Mathematics and
 System Sciences,
 Chinese Academy
 of Sciences, P.R.
 China

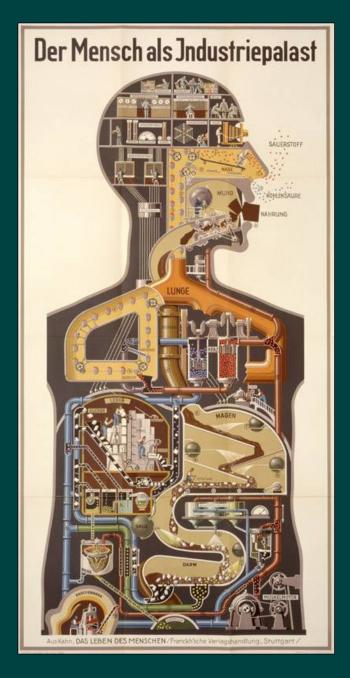




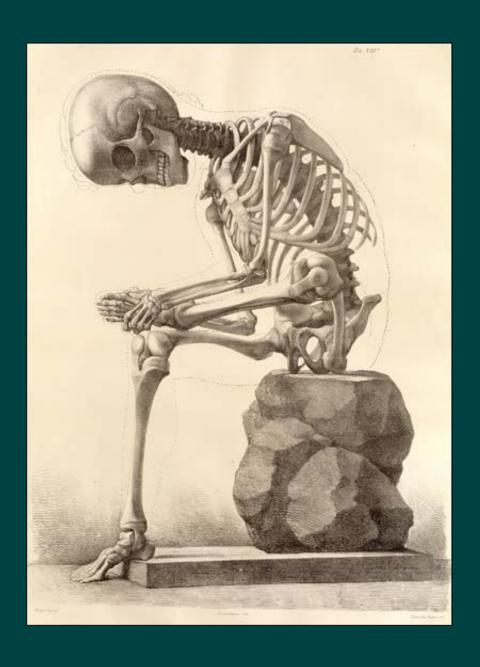
Govard Bidloo Gérard de Lairesse 1690



http://www.nlm.nih.gov/exhibition/dreamanatomy/index.html



Fritz Kahn 1926



Francesco Bertinatti Mecco Leone 1837-39

Outline

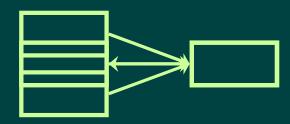
- ◆ Direct alignment
 - Concepts (FMA-GALEN)
 - Relationships
 - Cross-species (Human-Mouse)
- ◆ Indirect alignment through a reference ontology



Aligning Anatomical Concepts using Lexical and Structural Methods

Introduction

- ◆ Different representations of one domain
 - Formalism
 - Structure
 - Domain coverage
- ◆ Various approaches for comparing representations
 - Merging
 - Transformation
 - Alignment





Introduction

- Objective
 - Aligning two representations of anatomy
 - Foundational Model of Anatomy
 - GALEN common reference model
 - Beyond lexical comparison
 - Investigating reasoning capabilities
- ◆ Related work
 - P. Mork, et al., Challenges in precisely aligning models of human anatomy using generic schema matching

Noy NF. Tools for mapping and merging ontologies. In: Staab S, Studer R, editors. Handbook on Ontologies: Springer-Verlag; 2004. p. 365-384



Materials

Two representations of anatomy

• FMA

- Foundational Model of Anatomy
- University of Washington, 1994
- Conceptualization of the physical objects and spaces that constitute the human body

- ◆ GALEN common reference model
 - Generalized Architecture for Languages, Encyclopaedias and Nomenclatures in medicine
 - University of Manchester,1991
 - Development of a compositional and generative formal system for modeling all and only sensible medical concepts



FMA and GALEN

	FMA	GALEN
Underlying data model	Frame-based structure	Description logic
	Protégé-2000	GRAIL
Domain coverage	Anatomy	Medicine
Concepts	Pre-coordinated	Post-coordinated
	59,422	25,192
Synonyms	28,686	No
Anonymous concepts	No	3,176
Hierarchical relationships	is-a, part-of (6)	is-a, part-of (26)
Multiple inheritance	Yes	Yes
Associative relationships	Yes	Yes



Methods

Alignment steps

Lexical alignment

- Step 1: Acquiring terms
- Step 2: Identifying anchors (i.e., shared concepts)
 - lexically

Structural alignment

- Step 3: Acquiring (explicit and implicit) semantic relations
- Step 4: Identifying anchors structurally



Step 1: Acquiring terms

- **♦** Extracting concept names
 - FMA
 - Preferred concept names
 - Uterine tube
 - Synonyms
 - Oviduct
 - GALEN
 - Non-anonymous concept names
 - RoundLigamentOfUterus
 - * Not considered: anonymous concepts
 - (BodyStructure which < HasDivision Muscle >)



Step 2: Identifying anchors lexically

- ◆ Comparing two systems at the term level
 - Exact match
 - Normalization
- ◆ Preferred concept names and synonyms
- ◆ Anchors (*i.e.*, shared concepts)
 - FMA: Fibularis tertius

(synonym: Peroneus tertius)

• GALEN: Peroneus Tertius



Step 3: Acquiring semantic relations

- **♦** Semantic relations
 - <concept₁, relationship, concept₂>
 - Hierarchical relationships: *is-a* and *part-of*
 - <*Arm, part-of, Proximal segment of upper limb>*
- Extracting the explicit relations
- Acquiring implicit knowledge
 - Complementing missing inverse relations
 - Augmenting relations embedded in concept names
 - Inferring relations from a combination of relations



Implicit knowledge Complementing

- ◆ Inverse relationships
 - is-a and inverse-is-a
 - part-of and has-part
- Most part-of relations not represented bidirectionally
 - <Arm, has-part, Humerus>
- Complementing the inverse relations
 - <Humerus, part-of, Arm>



Implicit knowledge Augmenting

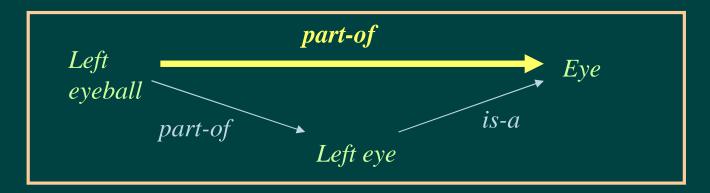
◆ Reification of *part-of* relationships

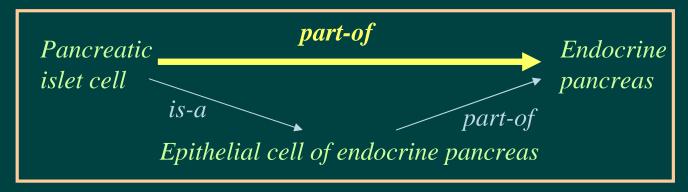
- ◆ Augmenting reified *part-of* relations
 - Reified: *Cardiac chamber, is-a, Subdivision of heart>*
 - No explicit (direct or indirect) *part-of* relationships between *Cardiac chamber* and *Heart* in FMA
 - Augmented: *<Cardiac chamber, part-of, Heart>*



Implicit knowledge Inferring

◆ Generating new inter-concept relationships by applying inference rules



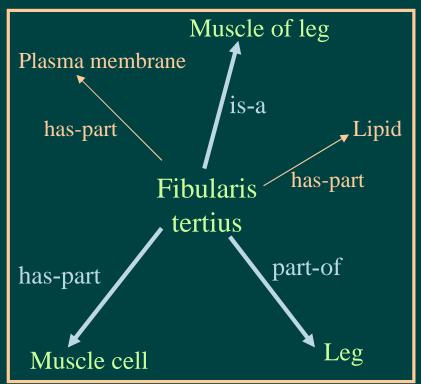




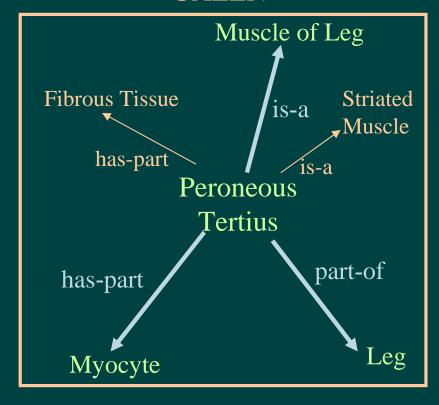
Step 4: Identifying anchors structurally

◆ Structural similarity: common relations among anchors

FMA



GALEN





Conflicts

- Conflicts: semantic incompatibility between anchors
 - Opposite type of links
 - FMA: Wall of heart has-part Apex of heart
 - GALEN: Heart Wall part-of Apex of Heart
 - Disjoint top-level categories
 - FMA: Foot is-a Anatomical structure



GALEN: feet is-a Unit



Results

Anchors identified by lexical alignment

- **♦** 2,353 anchors
 - 4 % of FMA concepts
 - 9 % of GALEN concepts



Semantic relations acquired

Types of relations	FMA	GALEN
Explicitly represented	238,135	214,403
Complemented	104,754	107,689
Augmented	315,860	27,274
Inferred	5,172,668	1,661,824
Total	5,831,417	2,011,190



Anchors identified by structural alignment

No evidence

Positive evidence

Negative evidence



Discussion

Explicit vs. implicit knowledge

- ◆ More positive structural evidence found for anchors
- ◆ Augmentation accounted for 74% of 523 anchors acquiring positive evidence
- ◆ More conflicting relations found for anchors



References

- ◆ Zhang S, Bodenreider O. Aligning representations of anatomy using lexical and structural methods. Proceedings of the First International Proceedings of AMIA Annual Symposium 2003:753-757.
 http://mor.nlm.nih.gov/pubs/pdf/2003-amia-sz.pdf
- ◆ Zhang S, Bodenreider O. *Knowledge augmentation for aligning ontologies: An evaluation in the biomedical domain*. Proceedings of the Semantic Integration Workshop at the Second International Semantic Web Conference (ISWC 2003) 2003:109-114. http://mor.nlm.nih.gov/pubs/pdf/2003-iswc-semint-sz.pdf



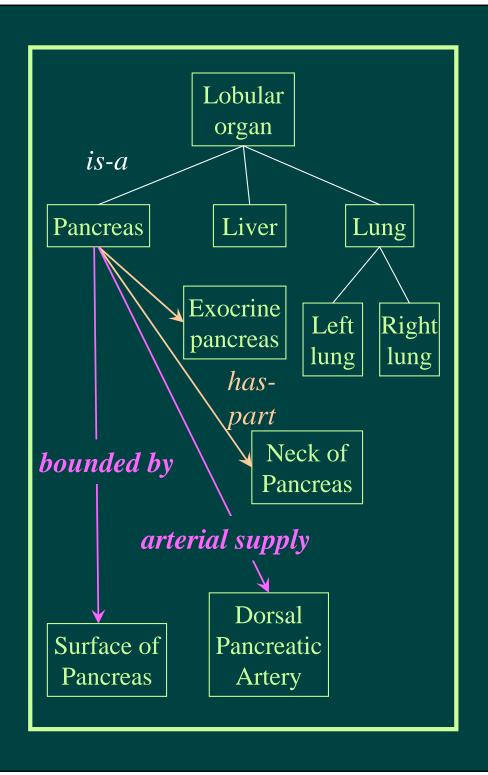
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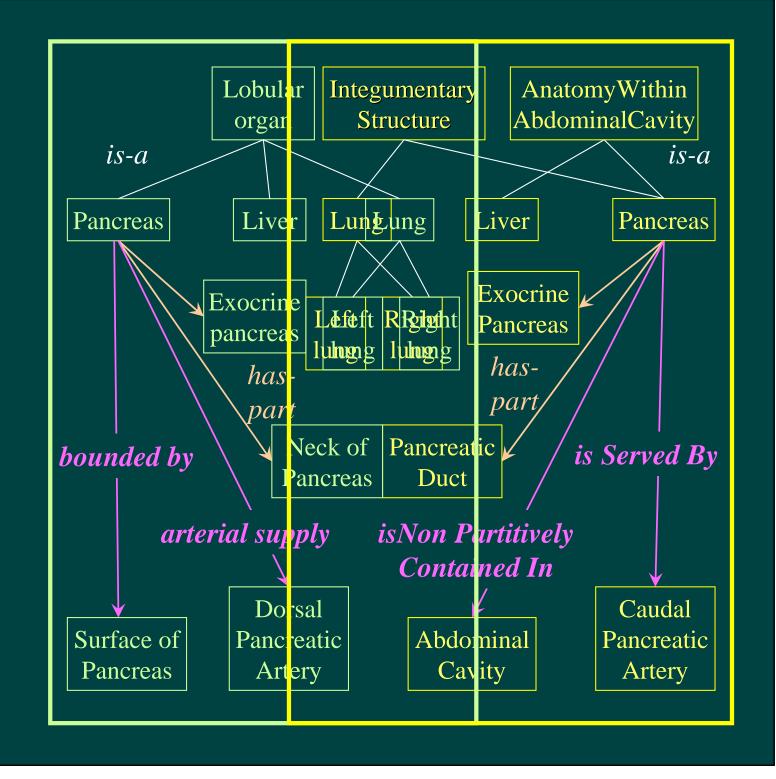
- ◆ Zhang S, Mork P, Bodenreider O. *Lessons learned from aligning two representations of anatomy*. Proceedings of the First International Workshop on Formal Biomedical Knowledge Representation (KR-MED 2004); 2004. p. 102-108. http://mor.nlm.nih.gov/pubs/pdf/2004-krmed-sz.pdf
- ◆ Zhang S, Bodenreider O. *Investigating implicit knowledge in ontologies with application to the anatomical domain*. Pacific Symposium on Biocomputing 2004: World Scientific; 2004. p. 250-261.

http://mor.nlm.nih.gov/pubs/pdf/2004-psb-sz.pdf



Comparing Associative Relationships among Equivalent Concepts across Ontologies





Introduction

- ◆ Few ontology merging / aligning tools deal with the issue of comparing associative relationships
- Our ontology aligning project
 - Two representations of anatomy
 - Foundational Model of Anatomy (FMA)
 - GALEN Common Reference Model
 - Aligning hierarchical relationships manually
 - Aligning concepts based on both lexical and hierarchical similarity



Introduction

- ◆ Objective: to identify equivalent expressions for associative relationships across ontologies
- **♦** Assumptions
 - Correspondence
 - between two relationships
 - between one relationship and a combination of relationships
 - Types of match
 - one-to-one
 - one-to-many
 - no match
 - Frequency of the correspondence



Materials

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FMA and GALEN

	FMA	GALEN
Underlying data model	Frame-based structure	Description logic
	Protégé-2000	GRAIL
Domain coverage	Anatomy	Medicine
Concepts	Pre-coordinated	Post-coordinated
	66,879	52,006
Hierarchical relationships	is-a, part-of (8)	is-a, part-of (40)
Inverses	inverse-isa, has-part	inverse-isa, has-part
Associative relationships	59	562
	Some have inverses	Every one has inverse
	branch of / branch	isBranchOf / hasBranch
	input from	isServedBy / serves

Methods

Comparing associative relationships

- ◆ NOT based on lexical similarity
- ◆ Based on previously identified equivalent concept pairs between FMA and GALEN
 - Share both lexical and hierarchical similarity
 - FMA: Pancreas has-part Exocrine pancreas
 - GALEN: Pancreas has-part ExocrinePancreas
 - Anchors (i.e., equivalent concepts across ontologies)
 - 2,604 pairs
 - 4% of FMA concepts and 5% of GALEN concepts



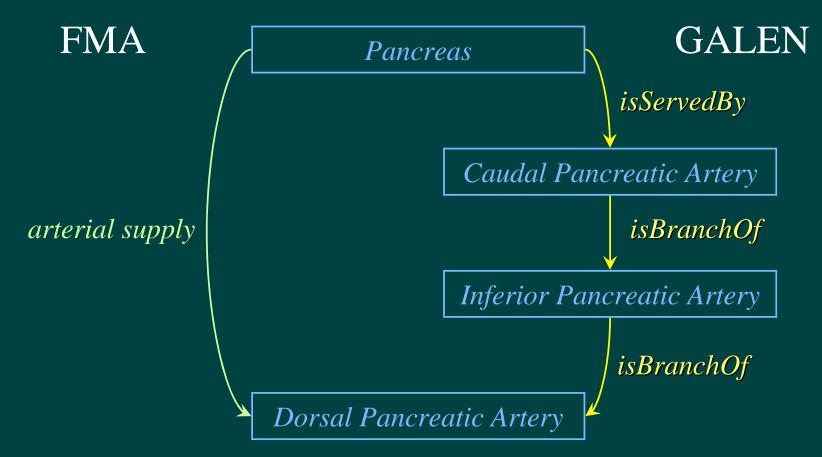
Step 1 Acquiring associative relations

- ◆ Associative relations: concept₁ relationship concept₂
- ◆ Extracting the explicit relations
 - Kidney isServedBy AutonomicNerveOfAbdomen
- ◆ Complementing the missing inverse relations
 - AutonomicNerveOfAbdomen serves Kidney
- Augmenting relations embedded in concept names
 - Explicit: Lateral cutaneous nerve of forearm branch-of Y branch-of Y is-a Branch of musculocutaneous nerve
 - Augmented: Lateral cutaneous nerve of forearm X is-a Branch of Y branch of Musculocutaneous nerve



Step 2 Identifying relationship patterns

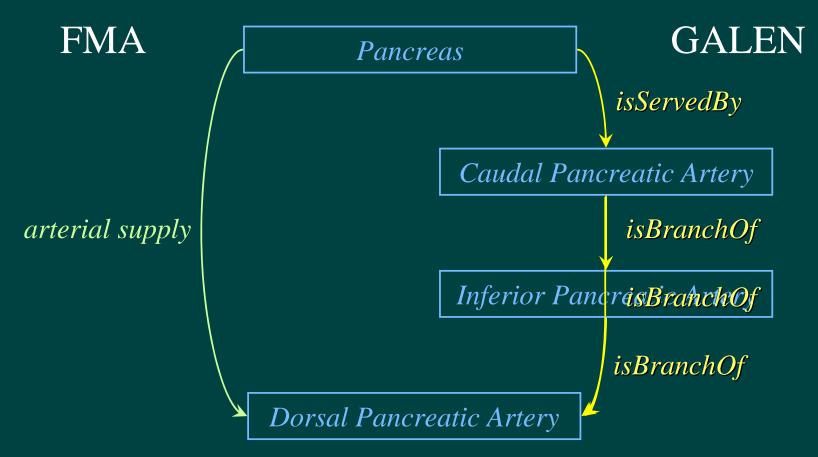
◆ Search for inter-anchor path pairs





Step 2 Identifying relationship patterns

Create relationship patterns from path pairs





Step 2 Identifying relationship patterns

- Create relationship patterns from path pairs
 - FMA: arterial supply

GALEN: isServedBy – isBranchOf

- Direct and indirect relationship patterns
- Frequency of relationship pattern
 - Number of path pairs sharing the pattern
 Number of all path pairs
 - Most frequent vs. accidental relationship patterns



Results

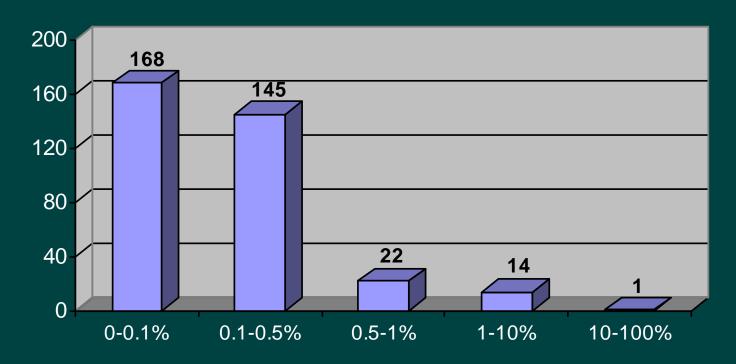
Associative relations acquired

Associative relations	FMA	GALEN
Explicit	18,688	288,732
Complemented	1,057	249,938
Augmented	1,838	108
Total	21,583	538,778
Between anchors	847	6,922



Path pairs and relationship patterns identified

- ◆ 4,070 inter-anchor path pairs
- ◆ 350 relationship patterns (47 direct and 303 indirect)







Examples of relationship patterns

FMA	GALEN	Frequency	
TIVIA	UALEN	(N =	4,070)
part-of	isBranchOf	518	13%
branch of	isBranchOf	310	8%
tributary of	isBranchOf	104	3%
member of	is-a	42	1%
nerve supply	part-of – isServedBy	16	0.4%
part-of – contained in	isNonPartitivelyContainedIn	10	0.25%
contained in	boundsSpace – inverse-isa	2	0.05%



Multiple matches

FMA	GALEN	Frequency $(N = 74)$	
arterial supply	isServedBy	18	24%
	isServedBy – isBranchOf		
	isServedBy – part-of	0.4	1.50/
	is Served By - is - a 34 4		46%
	isServedBy – inverse-isa		
	Other combinations	22	30%



Discussion

Analysis of relationship patterns

Types of patterns	Numb patte (N = 3	rns	Examples	Analysis
Associative corresponds to Associative	14	4%	F: tributary of G: isBranchOf	Equivalent associative relationships
Associative corresponds to Combination	303	87%	F: arterial supply G: isServedBy – is-a	Different levels of granularity or modeling choices
Associative and Hierarchical	33	9%	F: bounded by G: has-part	Not semantic equivalence

Semantic vs. lexical correspondence

- Semantically and lexically similar
 - 3 cases
 - {FMA: branch of, GALEN: isBranchOf}
- ◆ Semantically similar but lexically different
 - 11 cases
 - {FMA: arterial supply, GALEN: isServedBy}
- Semantically different but lexically similar
 - 4 cases
 - {FMA: bounded by, SALEN: isSpaceBoundedBy}



Limitations and future work

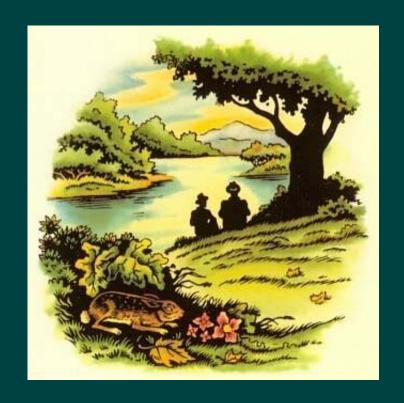
- ◆ Associative relationships do not exist in paths between anchors are not matched
 - 56% of FMA (e.g., fascicular architecture)
 - 84% of GALEN (e.g., is Positioned Distal To)
- Anchors used for identifying equivalent relationships have not been fully validated
- ◆ Take advantage of the equivalent relationships to discover more equivalent concepts



References

◆ Zhang S, Bodenreider O. Comparing associative relationships among equivalent concepts across ontologies. Medinfo 2004:459-463.
http://mor.nlm.nih.gov/pubs/pdf/2004-medinfo-sz.pdf





Aligning Mouse and Human Anatomies

Introduction

- ◆ Anatomy is central to the biomedical domain
- ◆ Comparing functional information about genes across model organisms requires aligned anatomies
- Objective: to align two ontologies of anatomy
 - Mouse anatomy
 Adult Mouse Anatomical Dictionary
 - Human anatomy
 Anatomy subset of NCI Thesaurus
- Contribution to the caBIG project



Materials

Adult Mouse Anatomical Dictionary (MA)

- Structured controlled vocabulary
- ◆ 2,404 concepts each identified by one name
 - Head/neck, Adrenal artery
- ◆ 259 synonyms
 - *Limb* has a synonym *Extremity*
- Directed acyclic graph
- ◆ Two relationships: *is-a* and *part-of*
- ◆ 38% concepts have no *is-a* relationship
 - Knee part-of Hindlimb
- ◆ 4% concepts have more than one *is-a* relationship
 - Hand phalanx is-a Phalanx
 is-a Hand digit bone



NCI Thesaurus (NCI)

- Standard vocabularies for cancer research
- Anatomy class
- ◆ Available in Ontology Web Language (OWL)
- ◆ 4,410 concepts, each having one preferred name
 - Abdominal esophagus
- ◆ 2,371 synonyms
 - Orbit has a synonym Eye socket
- ◆ Every concept has at least one *is-a* relationship
- ◆ 4% concepts have more than one *is-a* relationship
 - Radius bone is-a Long bone
 is-a Bone of the upper extremity
- ◆ Concepts are connected by a *part-of* relationship
 - Liver is physical part of Gastrointestinal system



MA and NCI

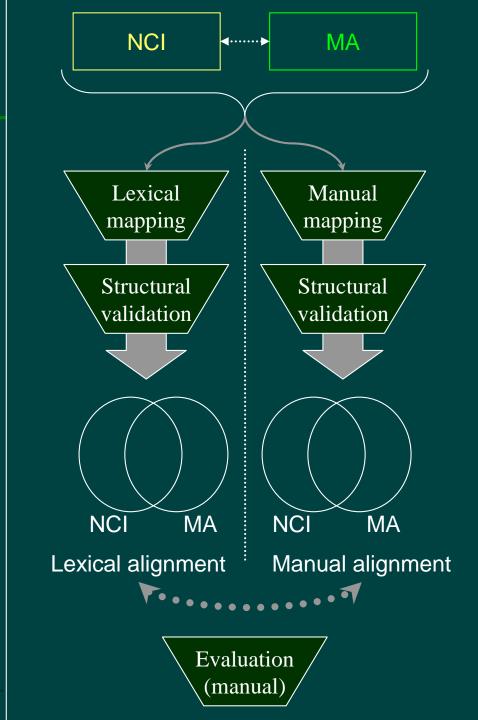
	MA	NCI
Underlying data model	Directed acyclic graph	Available in OWL
Domain coverage	Mouse anatomy	Human anatomy related to cancers
Concepts	2,404	4,410*
Synonyms	259	2,371
Hierarchical relationships	is-a, part-of	is-a, part-of
Inverses	-	-

^{*} Of which some 2000 correspond to entities not included in MA



Methods

Overview





Lister Hill National Center

Lexical approach

- ◆ Comparing two ontologies at the term level
 - Exact match
 - Match after normalization
- Preferred names and synonyms are used
 - MA: Forelimb

NCI: Upper extremity (synonym: Forelimb)

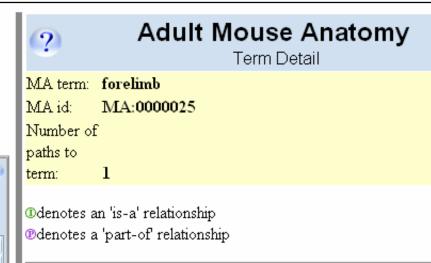
- UMLS synonymy is used to identify additional matches
 - MA: *Profunda femoris artery*

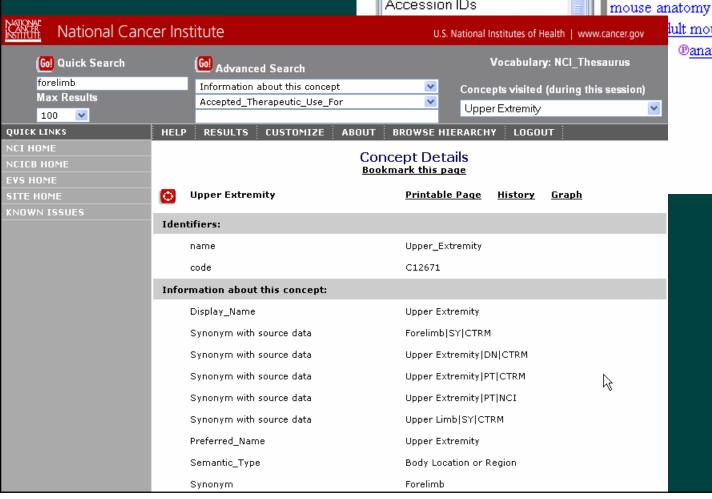
NCI: Deep femoral artery



Manual approach







tult mouse

@anatomic region

@limb

@forelimb [MA:0000025]

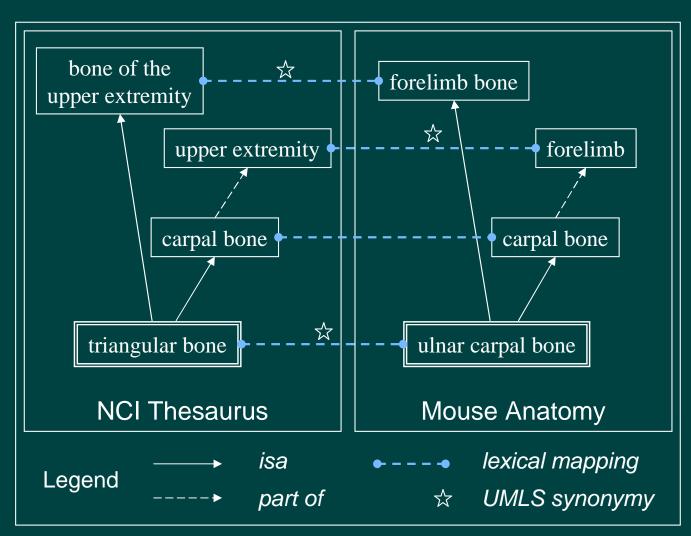
@arm +

@elbow +

@forelimb blood vessel +

@forelimb bone +

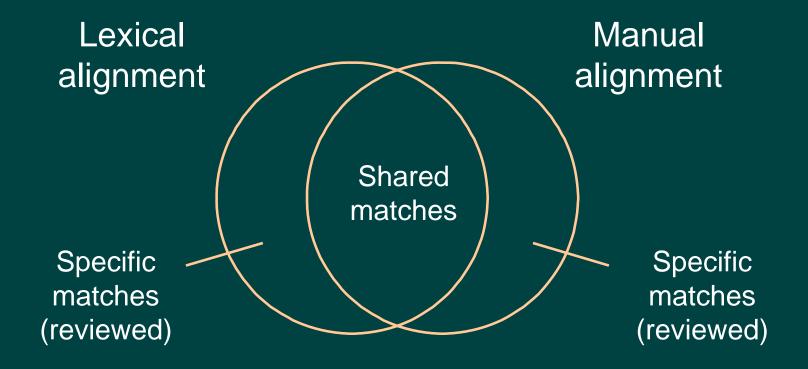
Validation by structural similarity



- Uses relations
 explicitly
 represented in
 each system and
 transitive
 closures
- Presence of relations to other anchors interpreted as structural evidence



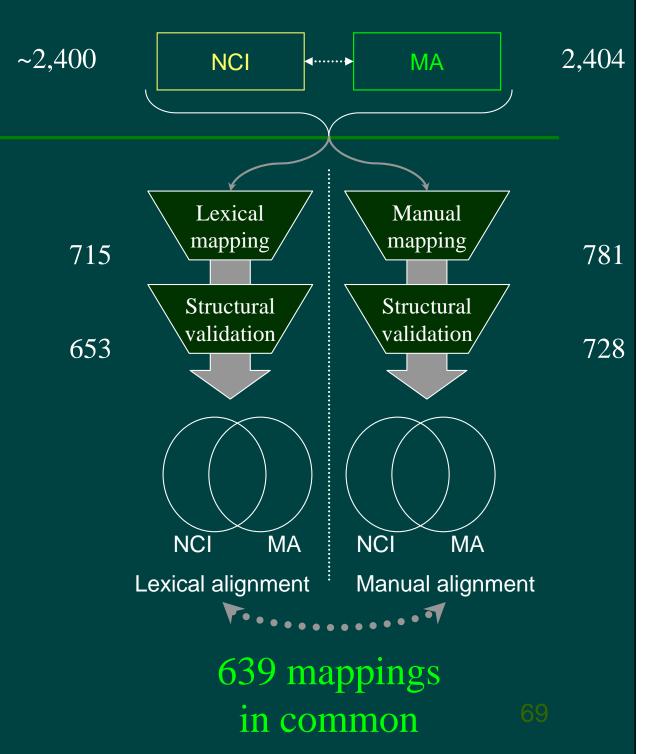
Evaluation



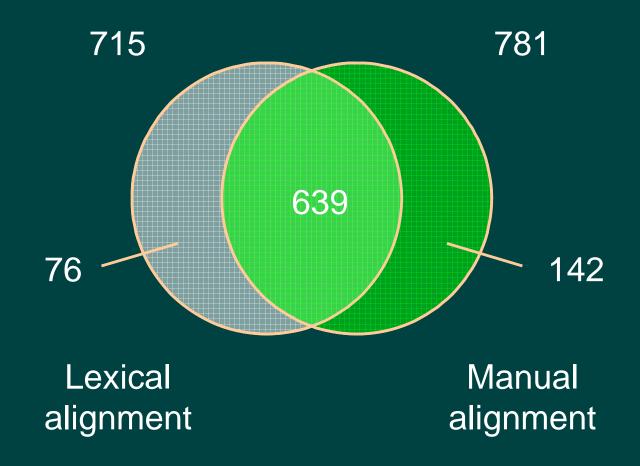


Results

Results



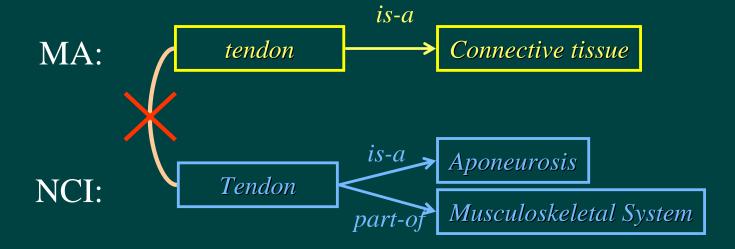
Comparison of the two alignments





Mappings identified by both approaches

- ◆ 639 mappings identified by both approaches
 - Most of them supported by structural evidence
 - {MA: *uterine cervix*, NCI: *Cervix Uteri*}
 - Some not supported by structural evidence
 - {MA: *tendon*, NCI: *Tendon*}





Mappings specific to the lexical approach

- ◆ 76 mappings specific to the lexical approach
 - Benefited from using UMLS synonyms
 - 61 valid mappings (80%)
 - {MA: *lienal artery*, NCI: *Splenic Artery*}
 - 15 invalid mappings
 - {MA: *cerebellum lobule I*, NCI: *Lingula of the Lung*}



Mappings specific to the manual approach

- ◆ 142 mappings specific to the manual approach
 - 133 valid mappings (94%)
 - {MA: alveolus epithelium, NCI: Alveolar Epithelium}
 - 9 invalid mappings
 - Human errors (coding)



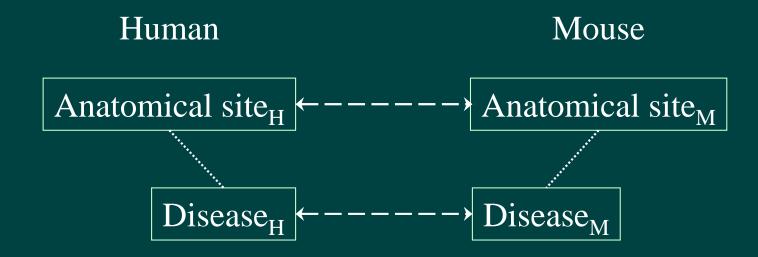
Discussion

Applications of the mapping for biologists

- ◆ Important for comparative science
 - Mouse models of human diseases e.g., emice.nci.nih.gov



♦ Example





Lessons learned

- Curated mapping
 - Only one expert
- ◆ Lexical approach
 - Large proportion of valid mappings
 - Including among mappings not supported by structural evidence (conservative approach)
- ◆ Manual approach
 - Can be supported by automated validation techniques (structural evidence), used to focus the attention of experts on potential problems



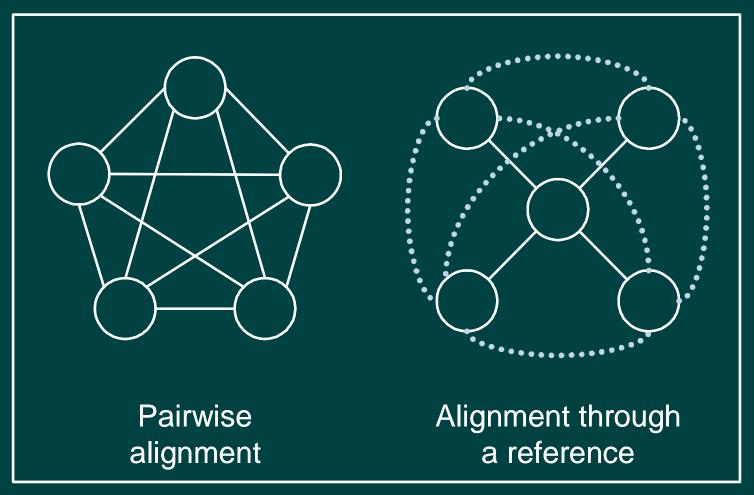
References

◆ Bodenreider O, Hayamizu TF, Ringwald M, de Coronado S, Zhang S. *Of mice and men: Aligning mouse and human anatomies*. Proceedings of AMIA Annual Symposium 2005:61-65. http://mor.nlm.nih.gov/pubs/pdf/2005-amia-ob.pdf



Indirect Alignment of Multiple Ontologies of Anatomy: through a Reference Ontology

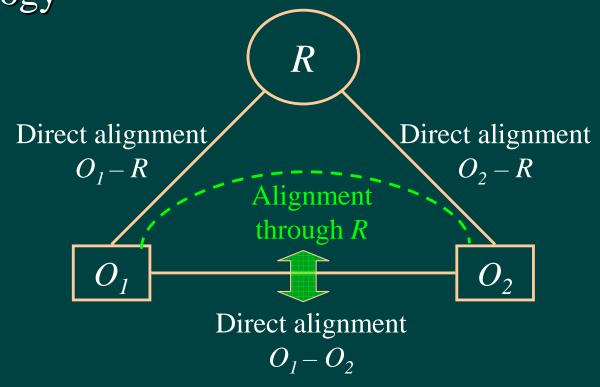
Approaches to aligning multiple ontologies





Introduction

◆ Objective: to investigate the indirect alignment of two anatomical ontologies through a reference ontology





Introduction

- ◆ Three ontologies of anatomy:
 - Adult Mouse Anatomical Dictionary (MA)
 - Anatomy subset of NCI Thesaurus (NCI)
 - Foundational Model of Anatomy (FMA)
- ◆ First attempt to automatically derive mappings among ontologies from their alignments to a reference ontology



Materials

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 - *Limb* has a synonym *Extremity*
- Directed acyclic graph
- ◆ Two relationships: *is-a* and *part-of*
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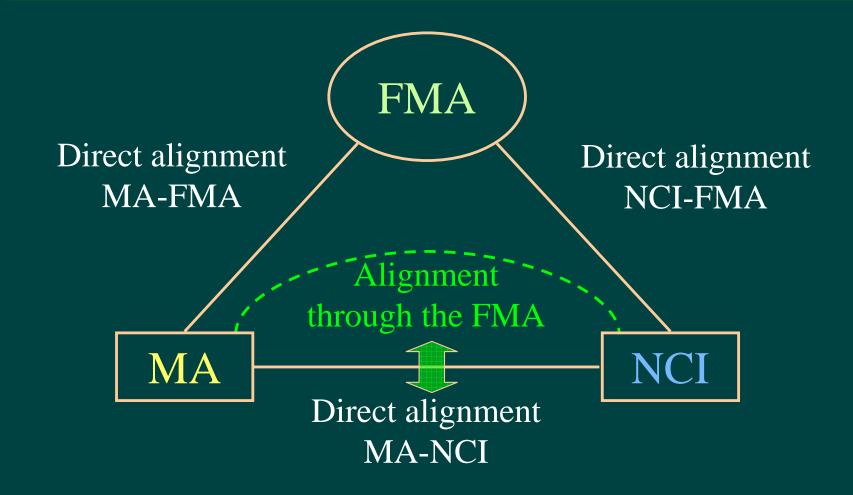
Foundational Model of Anatomy

- ◆ Conceptualize the physical objects and spaces that constitute the human body
- Frame-based structure in Protégé
- ◆ 71,202 concepts, each having one preferred name
 - Uterine tube
- **♦** 52,713 synonyms
 - *Uterine tube* has a synonym *Oviduct*
- ◆ Every concept has one and only one *is-a* relationship
- ◆ Seven *part-of* relationships and their inverses
 - constitutional part of and constitutional part
 - regional part of and regional part



Methods

Three phases





Phase 1 Direct alignment

Lexical alignment

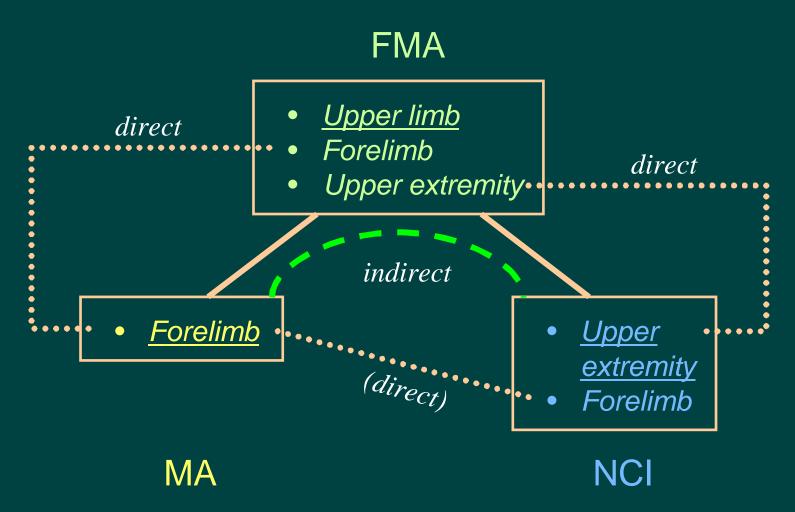
- Acquiring terms
- Identifying matches (i.e., shared concepts) lexically

Structural alignment

- Acquiring (explicit and implicit) semantic relations
- Identifying matches structurally

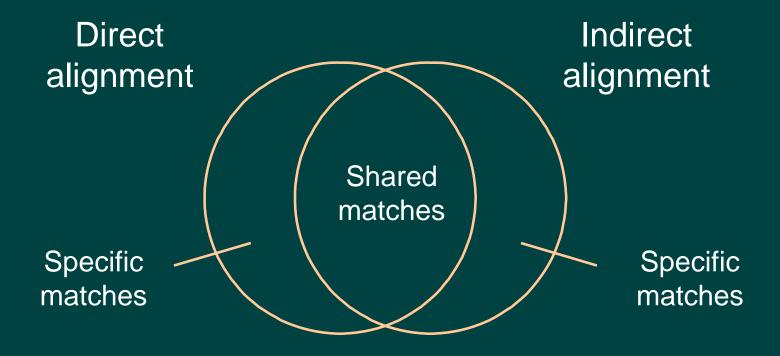


Phase 2 Indirect alignment





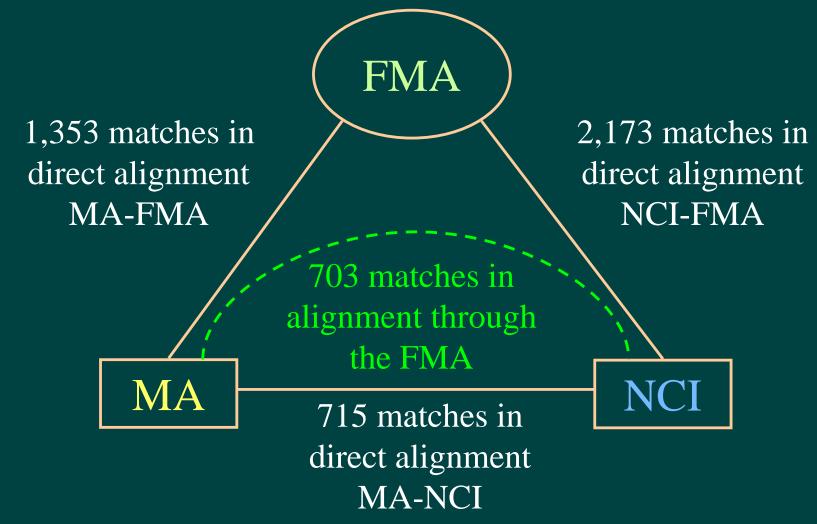
Phase 3 Comparison of two alignments





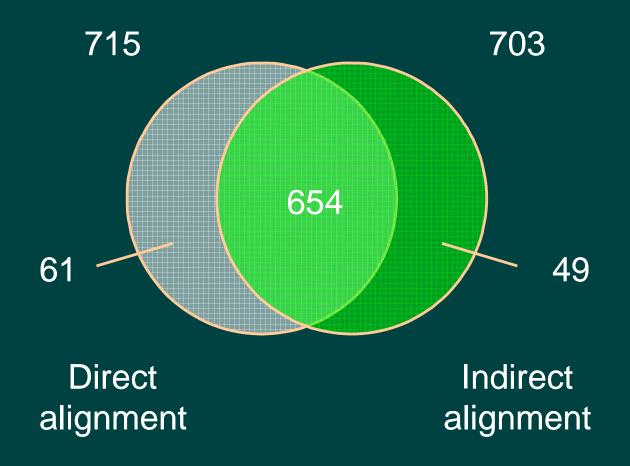
Results

Indirect alignment





Comparison of two alignments

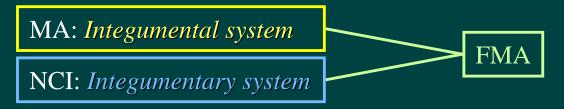




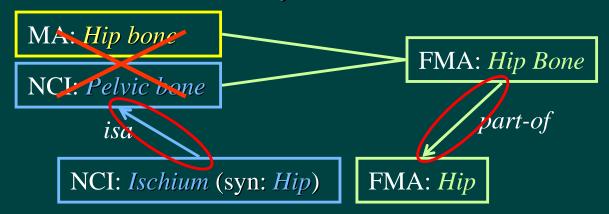
Discussion

Benefits of the indirect alignment

- ◆ Why are the 49 matches not identified in the direct alignment?
 - Additional synonyms by the FMA



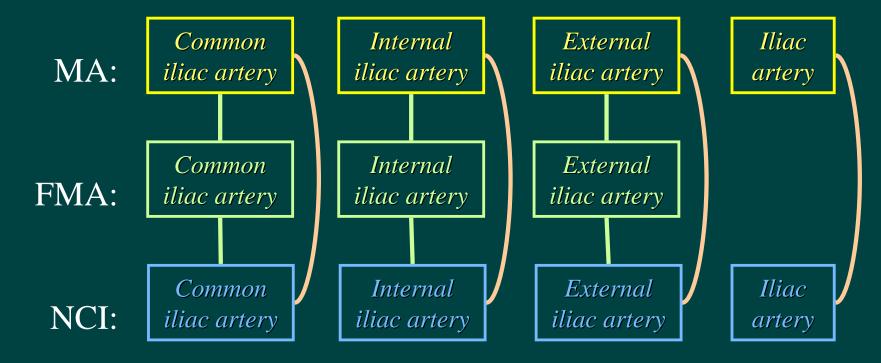
Additional relations by the FMA





Benefits of the direct alignment

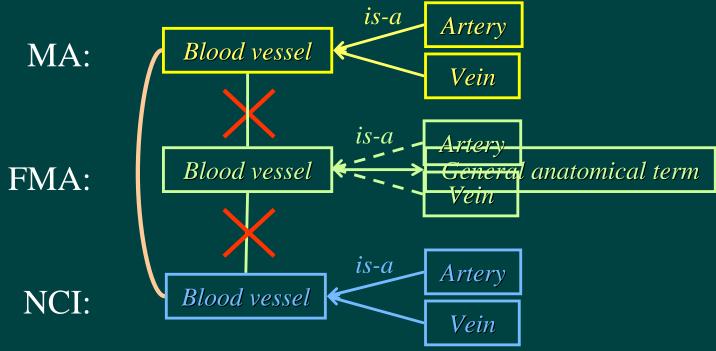
- Why are the 61 matches not identified in the indirect alignment through the FMA?
 - Different coverage





Benefits of the direct alignment

- ◆ Why are the 14 matches supported in the direct alignment while having no evidence in the indirect alignment through the FMA?
 - Different representation





Alignment through a reference vs. pairwise alignment

- ◆ Efficiency of alignment through a reference
 - n(n-1)/2 pairwise mappings
 - \bullet (n-1) mappings to a reference





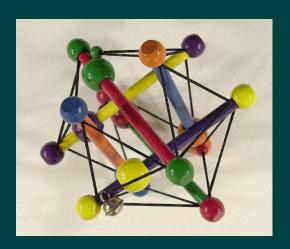
- Feasibility of alignment through a reference
 - Identified 91% of matches in the direct alignment
 - Identified additional matches not discovered by the direct alignment
 - Validated the FMA as a reference ontology



References

◆ Zhang S, Bodenreider O. Alignment of multiple ontologies of anatomy: Deriving indirect mappings from direct mappings to a reference. Proceedings of AMIA Annual Symposium 2005:864-868. http://mor.nlm.nih.gov/pubs/pdf/2005-amia-sz.pdf





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